REMARKS

In the Office Action, Claims 19-22, 24-26 and 28-31 remain withdrawn from consideration; Claims 2-8, 23 and 27 are rejected under 35 U.S.C. § 112, second paragraph; and Claims 2-8 have been rejected under 35 U.S.C. § 103.Claim 8 has been amended; Claims 32 and 33 have been newly added; and Claims 19-31 have been canceled. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**Versions with Markings to Show Changes Made**." Applicants respectfully submit that the rejections have been overcome or are improper in view of the amendments and/or for the reasons set forth below.

At the outset, 19-22, 24-26 and 28-31 remain withdrawn from consideration; and Claims 23 and 27 have been rejoined to the elected group of claims, namely, Claims 2-8. Although Applicants believe that Claims 19-22, 24-26 and 28-31 should be rejoined as well, in the spirit of cooperation, Applicants have canceled claims 19-31. In addition, Claims 32 and 33 have been newly added in place of Claims 23 and 27, respectively.

In the Office Action, Claims 2-8, 23 and 27 are rejected under 35 U.S.C. § 112, second paragraph. The Patent Office asserts that the term "approximately 2" of Claim 8 is unclear. Further, the Patent Office asserts that Claims 23 and 27 are dependent on a non-elected claim.

In response, Claim 8 has been amended to replace the term "approximately 2" with the term "2". Further, Claims 32 and 33 have been added in place of Claims 23 and 27 as previously discussed. Therefore, Applicants believe that the claimed invention fully complies with 35 U.S.C. § 112.

Accordingly, Applicants respectfully request that this rejection be withdrawn.

In the Office Action, Claims 2-8 are rejected under 35 U.S.C. § 103. More specifically, Claims 2-8 are rejected as being unpatentable over U.S. Patent No. 4,880,629 ("*Okamoto*") in view of U.S. Patent No. 5,039,609 ("*Klein*"); Claims 2-3 are rejected as being unpatentable over *Okamoto*, *Klein* and further in view of U.S. Patent No. 4,997,083 ("*Loretti*") or U.S. Patent No. 4,608,043 ("*Larkin*"); Claims 2-8 are rejected as being unpatentable in view of *Klein* and U.S. Patent No. 5,092,838 ("*Faict*"); Claims 2-3 are rejected as being unpatentable in view of *Klein* and *Faict* in view of *Loretti* or *Larkin*; and Claims 2-8 are rejected as being unpatentable in view of *Klein* and U.S. Patent No. 5,011,826 ("*Steudle*").

Applicants believe that the obviousness rejections are improper. In general, the present invention provides an improved dialysis solution. The improved dialysis solution provides for the use of specific polypeptides as an osmotic agent with an additional osmotic agent, such as dextrose. The inventors have found that selecting well defined polypeptides and utilizing same with an additional osmotic agent can overcome the disadvantages of using polypeptides alone or dextrose alone set forth on pages 10-26 of the Specification.

Of the rejected claims, Claims 2, 32 and 33 are the sole independent claims. Claim 2 recites a two part peritoneal dialysis solution designed to be mixed prior to infusion into a patient. The two part peritoneal dialysis solution includes, in part, a first part housed in a first structure and a second part housed in a second structure. The first part includes approximately 1.0 to about 8% (w/v) dextrose and a pH of approximately 4.0 to about 5.5; and the second part includes approximately 0.5 to about 8.0% (w/v) polypeptides and a pH of approximately 6.0 to about 7.5.

Claim 32 recites a two part peritoneal dialysis solution designed to be mixed prior to infusion into a patient. The two part solution includes a first part housed in a first structure including dextrose; and a second part housed in a second structure including approximately 0.25 to about 4.0% (w/v) polypeptides wherein either the first or the second structure includes a sufficient amount of the following ingredients so when the first part and second part are mixed, the following is provided: 120 to about 150 (mEq/L) sodium; 80.0 to about 110.0 (mEq/L) chloride; 0.0 to about 5.0 (mEq/L) lactate; 0.0 to about 45.0 (mEq/L) bicarbonate; 0.0 to about 4.0 (mEq/L) calcium; and 0.0 to about 4.0 (mEq/L) magnesium. Further, the two part solution includes not more than approximately 0.10% of the polypeptides having a molecular weight of greater than 1200, not more than approximately 25% of the polypeptides having a molecular weight of less than 400, and the weight average of polypeptides is within the range of approximately 400 to about 900 daltons.

Claim 33 recites a two part peritoneal dialysis solution designed to be mixed prior to infusion into a patient. The two part solution includes a first part housed in a first structure including dextrose; a second part housed in a second structure including approximately 0.25 to about 8.0% (w/v) polypeptides having a molecular weight average of approximately 400 to about 900 daltons; wherein the first or the second structure include a sufficient amount of the following ingredients so when the first part and second part are mixed, the following is provided: 120 to

about 150 (mEq/L) sodium; 80.0 to about 110.0 (mEq/L) chloride; 0.0 to about 5.0 (mEq/L) lactate; 0.0 to about 45.0 (mEq/L) bicarbonate; 0.0 to about 4.0 (mEq/L) calcium; and 0.0 to about 4.0 (mEq/L) magnesium. Further, the two part solution of Claim 33 requires that the first and second structures are two separate chambers of a single container.

At the outset, the Patent Office does not appear to give any patentable weight to the preamble of Claim 2 that recites a two part peritoneal dialysis solution designed to be mixed prior to infusion into a patient. In this regard, the Patent Office appears to argue that none of Claims 2 or 4-8 require that the two solutions be used on the same patient, that their use be recommended by the same physician or that the solutions are combined prior to infusion into a patient. See, Office Action, page 5.

Of course, the Court of Appeals for the Federal Circuit has held that "[i]n general, a preamble limits the claimed invention...if it is 'necessary to give life, meaning, and vitality' to the claim. *In re Cruciferous Sprout Litigation et al. v. Sunrise Farms et al.*, 2002 U.S. App. Lexis 17185, *8 (Fed. Cir. 2002) (quoting *Pitney Bowes, Inc. v. Hewlett-Packard Co.* 51 USPQ2d 1161, 1165 (Fed. Cir. 1999)). Further, "[c]lear reliance on the preamble during prosecution to distinguish the claimed invention from the prior art may indicate that the preamble is a claim limitation because the preamble is used to define the claimed invention." *Id.* at *8 and *9.

As applied, the Federal Circuit concluded that "both the specification and prosecution history indicate that the [preamble] phrase 'rich in glucosinolates' helps to define the claimed invention and is, therefore, a limitation of claim 1...". *Id.* at *9. The Federal Circuit relied on, for example, a stated objective of the invention to provide food products and food additives that are rich in cancer chemoprotective compounds, such as food products rich in glucosinolates. Moreover, the Federal Circuit pointed to arguments raised during examination that relied on the preamble language in response to an anticipation rejection. *Id.* at *9 and *10.

As in this case, the specification and examination process to date clearly support Applicant's position that the preamble language "designed to be mixed prior to infusion into a patient" of Claim 2 should be given proper patentable weight. For example, an advantage of the present invention is that it provides a balanced supplementation of polypeptides (protein source) and dextrose (energy source) through a dialysis solution to improve the nutritional status of a renal patient. See, Applicant's Specification, p. 8. Further, Applicants have and continue to

argue during the examination of the present application that the two part peritoneal dialysis solution of Claim 2 includes a dextrose-based part and a polypeptide-based part that are mixed prior to infusion into a patient during peritoneal dialysis and that the two part solution of the claimed invention is clearly patentable over the purported solutions disclosed in the cited art. Therefore, Applicants believe that the preamble language "designed to be mixed prior to infusion into a patient" of Claim 2 should be given proper patentable weight.

With respect to the prior art rejections, the Patent Office relies on the *Klein* reference in support of each of the obviousness rejections. Yet, *Klein* does not disclose that peptide solutions should be present in a container which is in proximity to a second container which contains glucose as even admitted by the Patent Office. See, Office Action, page 4. The clear emphasis of *Klein* relates to osmotically active agents used in peritoneal dialysis solutions that substitute polypeptides for dextrose. Indeed, *Klein* discloses that it provides "an osmotic agent which is not only a safe and beneficial alternative to glucose, but which also is economically feasible." See, *Klein*, col. 3, lines 53-57. Moreover, at best, *Klein* only generally discloses that the peptides can be combined with an osmotically balanced aqueous solution. This is clearly deficient with respect to the claimed invention which relates to improved dialysis solutions that include specific amounts of peptides in combination with dextrose as an osmotic agent.

Moreover, Applicants question why the Patent Office considers that the peptide mixtures disclosed in *Klein* are "quite different from whey protein hydrolysates *per se*." See, Office Action, page 4. Indeed, *Klein* discloses that the peptide mixtures can be readily prepared by hydrolysis of larger proteins, most preferably milk whey proteins. See, *Klein*, column 5, lines 24-25; column 6, lines 33-35. In this regard, Applicants' experimental tests (e.g., Examples 1 and 2) are clearly relevant and thus demonstrate the advantages of the present invention over *Klein*.

For example, the test Example 1 was conducted to evaluate the peptides disclosed in European Patent No. 0218900 (equivalent to *Klein*) as alternative osmotic agents to dextrose in dialysate solutions. Further, Example 2 sets forth irritation screening that was conducted on a variety of solutions. Applicants believe that the above examples (Example Nos. 1 and 2) demonstrate that the use of only a polypeptide mixture, such as that set forth in *Klein*, is not clinically acceptable in a peritoneal dialysis solution.

In order for the polypeptide composition of *Klein* to obtain the absorption equivalent to a 2.5% dextrose solution, one needs at least a 5.5% polypeptide solution. However, Example No. 1 demonstrates that the absorption of the polypeptide is at least 50% to 60%. If polypeptides, at an at least 5% concentration in a dialysis solution are used at every exchange, the patient would receive at least 200 grams of amino acids per day. It has been found that peritoneal absorption of more than 40 grams of amino acids per 24 hours can cause uremia in dialysis patients.

Accordingly, due to the absorption characteristics of the polypeptides, it has been determined that preferably only a 1% to 2% concentration of a polypeptide solution, such as *Klein*, should be used. However, at such a concentration, the polypeptides do not provide a sufficient osmotic agent. It has also been found that in order to control uremia problems, it is necessary to control the proportion of lower molecular weight peptides.

Example No. 2 demonstrates that the polypeptides of *Klein* have the potential for immunogenicity. The problem stems from the fact that too great a proportion of peptides in *Klein* have a molecular weight above 1200. It has been found that not more than 0.10% of the polypeptides should have a molecular weight of greater than 1,200.

Accordingly, pursuant to the present invention, the polypeptides are used in a specific concentration of, for example, about 1% to about 8% with an osmotic agent, such as dextrose in a concentration of 0.5% to 8%. Further, the polypeptides of the claimed invention can have an average molecular weight of about 400 to about 900 daltons.

This can minimize the risk of immunogenic response. Additionally, not more than 25% of the polypeptides should have a molecular weight of less than 400. This prevents the uremic problems that will occur with the solution proposed in *Klein*. Further, the polypeptide solutions of *Klein* have the potential of producing allergic reactions, due to the size of the polypeptides used in solution. In contrast, the claimed polypeptides have a size that will not produce such allergic reactions. Therefore, Applicants believe that the two part peritoneal dialysis solutions of the claimed invention require a specific composition including specific amounts of polypeptides and dextrose that can be used in peritoneal dialysis to overcome the disadvantages of *Klein*.

Even if combinable, the other cited art does not appear to remedy the deficiencies of *Klein*. In this regard, the Patent Office merely relies on the other cited art for their alleged and general teachings regarding peritoneal dialysis solutions that include glucose. For example, *Okamoto* merely relates to dialytic solutions that contain glycerol and monosaccharides as

osmotic pressure regulating agents for regulating the osmotic pressure necessary for the removal of water. See, *Okamoto*, col. 5, lines 15-20.

With respect to the alleged teaching of *Steudle*, Applicants respectfully submit that the mere mention of a combination of peptide with glucose in the same sentence is not sufficient grounds for an obviousness rejection contrary to the Examiner's position. See, *Steudle*, col. 4, lines 51-59. Moreover, *Steudle* does not remedy the deficiencies of *Klein* with respect to the polypeptide features of the claimed invention. *Steudle* does not even provide any description of peptides that can be used as osmotic agents.

Indeed, *Steudle* does not define the circumstances wherein one would mix peptides with an osmotic agent, such as dextrose as required by the claimed invention. Instead, *Steudle* merely relates to the use of galactose as an osmotic active substance. In attempting to provide as broad a disclosure as possible, the *Steudle* patent makes a backhanded reference to peptides in column 4, line 58, along with an exhaustive list of the groups of possible osmotic agents to be used in addition to galactose and glucose.

With respect to the remaining references, the Patent Office merely relies on *Faict* for its alleged teaching regarding a two part dialysis mixture that contains glucose in one part, and histidine, or oligomers thereof, in another. Further, the Patent Officer merely relies on *Loretti* and *Larkin* for their alleged teachings regarding sterile containers which include two different chambers for mixing solutions. Therefore, Applicants do not believe that one skilled in the art would be inclined to modify *Klein* in view of same to arrive at the claimed invention.

At best, the cited art, even if combinable, simply provides "general guidance" as to the particular form of the claimed invention. Absent a suggestion, teaching or motivation of the specific compositions of the two part peritoneal dialysis solutions including polypeptides and dextrose claimed in the present invention, Applicants respectfully submit that the Patent Office has impermissibly applied hindsight reasoning in support of the prior art rejections.

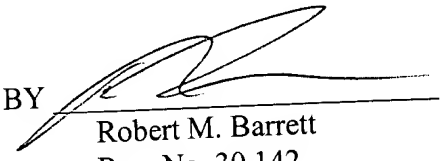
Based on the apparent differences between the cited art and the claimed invention, Applicants believe that the cited art fails to disclose or suggest a number of features of the claimed invention. Therefore, Applicants respectfully submit that the cited art, even if combinable, fails to render obvious the claimed invention.

Accordingly, Applicants respectfully request that the obviousness rejections with respect to the claimed invention be withdrawn.

For the foregoing reasons, Applicants respectfully request reconsideration of their patent application and earnestly solicit an early allowance of same.

Respectfully submitted,

BELL, BOYD & LLOYD LLC

BY 

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 8 has been amended as follows:

8. (Amended) The two part peritoneal dialysis solution of Claim 2 wherein the synthetic polypeptides are ~~approximately~~ 2 to about 15 amino acids long.

Claims 19-31 have been cancelled.

Claims 32 and 33 have been added.